REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the following commentary. With the changes set forth above, claims 23, 25, 26 , 29 and 30 are pending.

Objections

The Examiner and draftsperson have objected to Figure 1 as filed. Applicants submit a new formal drawing of Figure 1 and believe this obviates the Examiner's objection.

The Examiner also objects to the oath/declaration as originally filed. Examiner has requested a petition under 37 C.F.R. § 1.47 and 37 C.F.R. § 1.183. Because Rule 1.47 is inapplicable to the present case and, hence, a petition under Rule 183 is unnecessary, Applicants request that the Examiner withdraw this objection. In the alternative, Applicants are submitting a Rule 183 petition to the Petitions Branch, along the lines suggested by the Examiner.

All of the named inventors executed the original declaration, and the Office granted the present application a filing date. Under these circumstances, 37 C.F.R. § 1.47 appears inapplicable, as the filing date was granted and all inventors were available.

The Examiner also has requested under 37 C.F.R. § 1.67 that the inventors submit a new declaration, due to deficiencies under 37 C.F.R. § 1.52(c). Rule 67 makes that a discretionary matter; *i.e.*, the Office **may** make such request. Applicants have made diligent efforts to obtain the supplemental declaration without success, as described in the Declaration of Julia Andral-Ziurys, which was filed with a response dated December 7, 2001. Applicants also believe that Rule 52(c) is directed to application papers other than the oath or declaration. Rule 52(c) is directed specifically to alterations made to application papers before the signing of the oath or declaration, not to alterations made in the oath or declaration. Because the Examiner ***may*** make a request to file a supplemental declaration and because Rule 52 is inapplicable, Applicants request that the Examiner withdraw the objection in question.

Finally, the Examiner objected to the specification where SEQ. ID. NO. 1 is used to describe an amino acid sequence. This objection should be withdrawn because the Examiner's express concern is inapposite to the present specification.

Rejections under 35 U.S.C. § 112

The present claim revisions render moot all the rejections made by the Examiner in the last official action, perhaps excepting the rejection of claim 26 under 35 U.S.C. § 112, first paragraph.

In the latter regard, the Examiner acknowledges that antibodies can be prepared against a polypeptide modified by substitution of one or more amino acids but contends that the application does not include descriptive support for a specific variant of the 27-427 peptide of SEQ. ID. NO. 2 which specifically binds to the 64G12 monoclonal antibody. Thus, the Examiner considers claim 26 to lack support in the specification and, hence, the claimed peptides or polypeptides to constitute new matter. Applicants respectfully disagree.

These derived peptides are described in the application as filed, at least at page 8, last paragraph. Indeed, Examiner acknowledges this paragraph which mentions the fact that the amino acid sequence 1-229 of SEQ. ID. NO. 2 is an advantageous peptide of the invention, and that *antibodies* also can be prepared against a *polypeptide modified by substitution of one or more amino acids*, provided that the modified polypeptide is recognized by antibodies directed against the non modified extracellular domain of the IFN-R.

The skilled artisan, at the date of filing of the present application, knew that some modifications could be made to peptides without modifying their immunologic specificity. Applicants have described the structural characteristics (e.g., length and amino acid sequence) and functional characteristics (e.g., binding specificity) of the native peptide or polypeptide, and a skilled artisan is capable of making the conservative substitutions as disclosed in page 8 of the specification. For example, one of ordinary skill in the art understands conservative substitutions, wherein an amino acid is replaced by another amino acid having similar properties with respect to hydrophobicity, polarity,

charge and steric hindrance, can be silent with regard to the immunologic properties of the peptide, especially if the substitutions are made in a region which is not exposed at the surface of the peptide.

Furthermore, Applicants emphasize that the specification discloses a particular monoclonal antibody that can be used to bind to the substituted peptide. The last paragraph on page 8 discussing substituted peptides is directed to "monoclonal antibodies according to the invention," which would include monoclonal antibody 64G12. The artisan seeking to obtain a polypeptide within the extracellular region of IFN-R with conservative substitutions would know from Applicants' teachings to use the available monoclonal antibody 64G12 and the teachings of the present specification to readily obtain the claimed polypeptides. Indeed, one of ordinary skill in the art could easily produce peptides derived from those claimed by substituting one or more amino acid residues and testing the modified peptide's ability to specifically bind monoclonal antibody 64G12. As explained above, it is expected from known principles that such mutations would not affect the immunological properties of the peptide, especially if the substitution involved amino acids having similar hydrophobicity, charge and steric hindrance and the substitution occurred outside of an epitope. For these reasons, Applicants believe that present claim 26 is supported by the specification as filed, and that the modified polypeptide does not constitute new matter.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 1 August 2002 By S. A. Bent

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Version with Markings to Show Changes Made

In the Specification:

Please amend the specification as follows:

On page 8, replace the 3 full paragraph spanning lines 15-21 with the one submitted herein.

> Monoclonal antibodies of the invention can for example be prepared against the soluble form of the receptor. A hydrosoluble polypeptide corresponding to the soluble form of the INF-R is described on figure 2 of SEQ ID NO[**S**]: [1-]2. According to the present invention, a soluble form of the IFN-R corresponds to a peptide or a polypeptide, capable of circulating in the body.

On page 8, replace the fourth full paragraph spanning lines 22-33 with the one submitted herein.

> Other monoclonal antibodies according to the invention can also be prepared against a peptide comprised in the extracellular domain of the receptor as described in figure 2 SEQ ID NO[**S**]: [1-]2. An advantageous peptide corresponds for instance to the amino_acid sequence comprised between amino_acid 1 and amino_acid 229 of SEQ ID NO: [**1 or**]2. According to another embodiment of the invention, the antibodies can be prepared against a polypeptide modified by substitution of one or more amino acids, provided that antibodies directed against the non modified extracellular domain of the IFN-R, recognize the modified polypeptide or peptide.

On page 10, replace the third full paragraph spanning lines 11-16 with the one submitted herein.

> One particular antibody satisfying the requirements of the invention, is such as it directed against an epitope on the amino_[-]acid sequence comprised between amino_[-]acid 27 and amino_[-]acid 427 of the extracellular domain of the human IFN-R as represented on figure 2 SEQ ID NO**[S]**: **[1-]**2.

On page 14, replace the first full paragraph spanning lines 4-13 with the one submitted herein.

> A fragment of DNA containing the sequence coding for the extracellular domain (amino acids 27 to 427) of the human INF-R (figure 2 SEQ ID NO**[S]**: **[1-]**2), in which an extra-sequence coding for 5 histidyl residues was introduced just before the termination codon, was cloned in the expression vectors pKK233-2. This fragment was produced by the Polymerase Chain Reaction (PCR) and the resulting plasmids were sequenced to confirm both in-frame insertion with the Shine-Dalgarno sequence and the appropriate sequence coding for the receptor.

In the Claims:

23. (Fifth Amendment) An isolated peptide or polypeptide which is a fragment of the extracellular portion of the interferon receptor (IFN-R) of SEQ ID NO: 2, said peptide or polypeptide consisting of an amino acid sequence from position 27 to position 427 of SEQ ID NO: 2 **[or a portion thereof]**; wherein said peptide or polypeptide **[or a portion thereof]** specifically binds to monoclonal antibody 64G12 deposited at the ECACC under no. 92022605.

25. (Fifth Amendment) An isolated peptide or polypeptide which is a fragment of the extracellular portion of the interferon receptor (IFN-R) of SEQ ID NO: 2, said peptide or polypeptide consisting of an amino acid sequence from position 1 to position 229 of SEQ ID NO: 2 **[or a portion thereof]**; wherein said peptide or polypeptide **[or a portion thereof]** specifically binds to monoclonal antibody 64G12 deposited at the ECACC under no. 92022605.

26. (Fourth Amendment) An isolated peptide or polypeptide which is derived from a peptide or polypeptide as claimed in claim 23 **or 25** by substitution of one or more amino acid residues and which retains the ability to specifically bind to monoclonal antibody 64G12 deposited at the ECACC under no. 92022605.